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(FILE 'HOME' ENTERED AT 16:03:40 ON 17 SEP 2005)

FILE 'REGISTRY' ENTERED AT 16:03:45 ON 17 SEP 2005

L1 1 S OLANZAPINE/CN  
L2 0 S OLANZAPINE/CRN  
L3 7 S OLANZAPINE?  
L4 521 S C17 H18 N4 O S/MF  
L5 1 S L3 AND L4  
L6 237 S C17 H20 N4 S/MF  
L7 1 S L6 AND L3  
L8 1 S METHANOL/CN  
L9 1 S ETHANOL/CN  
L10 2 S PROPANOL/CN  
L11 2 S BUTANOL/CN  
L12 2 S PENTANOL/CN  
L13 3 S HEXANOL/CN  
L14 1 S ISOPROPANOL/CN  
L15 1 S TERT-BUTANOL/CN  
L16 1 S SEC-BUTANOL/CN  
L17 1 S ISOBUTANOL/CN  
L18 1 S ISOPENTANOL/CN  
L19 3 S SEC-PENTANOL/CN  
L20 1 S TERT-PENTANOL/CN  
L21 1 S ISOHEXANOL/CN  
L22 1 S SEC-HEXANOL/CN  
L23 1 S TERT-HEXANOL/CN  
L24 23 S L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR

FILE 'CAPLUS' ENTERED AT 16:16:54 ON 17 SEP 2005

L25 35 S L7 AND L24

=> s l7 and form vi

1388 L7  
1454571 FORM  
556021 FORMS  
1876257 FORM  
(FORM OR FORMS)  
207513 VI  
52788 VIS  
260019 VI  
(VI OR VIS)  
385 FORM VI  
(FORM(W)VI)

L26 1 L7 AND FORM VI

=> s l25 or l26

L27 36 L25 OR L26

=> d ibib abs hitstr total

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107 ANSWER 1 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:735332 CAPLUS

DOCUMENT NUMBER: 143:199900

TITLE: Composition comprising salts or hydrates or polymorphs of idazoxan or its derivatives

INVENTOR(S): Bougaret, Joel; Avan, Jean-Louis; Segonds, Roland

PATENT ASSIGNEE(S): Pierre Fabre Medicament, Fr.

SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 722,451.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005176798	A1	20050811	US 2004-974675	20041028
FR 2861299	A1	20050429	FR 2003-12626	20031028
US 2005090537	A1	20050428	US 2003-722451	20031128
PRIORITY APPLN. INFO.:			FR 2003-12626	A 20031028
			US 2003-722451	A2 20031128

AB The present invention discloses a pharmaceutical composition comprising idazoxan or derivs. and their therapeutically acceptable salts, racemates, optically active isomers and polymorphs. Thus, a tablet was prepared comprising idazoxan hydrochloride 20%, microcryst. cellulose 10%, glyceryl behenate 5%, colloidal silica 0.1% and lactose monohydrate to 100%. The addition of idazoxan to the treatment with fluphenazine in patients with schizophrenia to control extrapyramidal symptoms led to significant reduction in the symptoms in comparison with fluphenazine monotherapy.

IT 64-17-5, Ethanol, processes 71-36-3, Butanol, processes  
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)  
(composition comprising salts or hydrates or polymorphs of idazoxan or its derivs.)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

RN 71-36-3 CAPLUS

CN 1-Butanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-OH

IT 132539-06-1, Olanzapine

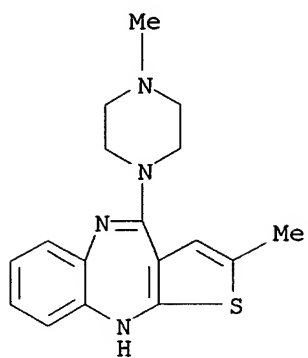
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in combination with; composition comprising salts or hydrates or polymorphs of idazoxan or its derivs.)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)

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ANSWER 2 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:638703 CAPLUS

DOCUMENT NUMBER: 143:139194

TITLE: Buccal dosage forms for extended drug release

INVENTOR(S): Jain, Rajesh; Jindal, Kour Chand; Singh, Sukhjeet

PATENT ASSIGNEE(S): Panacea Biotec Ltd., India

SOURCE: PCT Int. Appl., 25 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005065640	A1	20050721	WO 2005-IN3	20050105
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: IN 2004-DE24 A 20040106

IN 2004-DE26 A 20040106

AB Buccal dosage form compns., preferably of poorly bioavailable drug(s), or drug(s) which undergo extensive presystematic metabolism, are provided. The compns. provide extended release of the drug in the oral cavity, and are preferably in the taste masked form. A process of preparing of such compns. is also provided. Thus, a tablet contained sumatriptan succinate 25.0, Indion-204 75.0, maltodextrin 48.0, sucrose 30.0, CM-cellulose 18.0, HPMC 8.0, HPC 8.0, citric acid 15.0, NaCl 5.0, and Povidone 3.0 25 mg/tablet.

IT 64-17-5, Ethanol, uses 67-63-0, Isopropanol, uses

RL: NUU (Other use, unclassified); USES (Uses)

(buccal dosage forms for extended drug release)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

RN 67-63-0 CAPLUS

CN 2-Propanol (9CI) (CA INDEX NAME)

OH  
|  
H<sub>3</sub>C-CH-CH<sub>3</sub>

IT 132539-06-1, Olanzapine

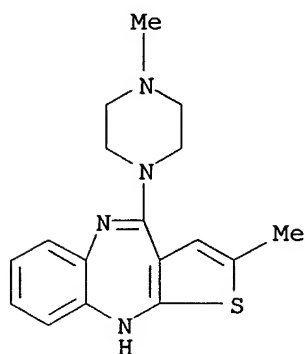
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(buccal dosage forms for extended drug release)

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RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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~~107~~ ANSWER 3 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:471959 CAPLUS

DOCUMENT NUMBER: 143:1313

TITLE: Use of cyclooxygenase-2 selective inhibitors and combinations with neuroleptics for the treatment of schizophrenic disorders

INVENTOR(S): Hagan, James; Routledge, Carol

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049034	A2	20050602	WO 2004-EP13076	20041117
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: GB 2003-26967 A 20031119

GB 2003-27937 A 20031202

OTHER SOURCE(S): MARPAT 143:1313

AB The invention discloses the use of compds. which are cyclooxygenase-2 (COX-2) inhibitors, and pharmaceutically acceptable salts and solvates thereof, for the treatment of schizophrenic disorders. Schizophrenic disorders of the invention are to be intended schizophrenia, delusional disorders, affective disorders, autism or tic disorders, schizophreniform disorders, in particular chronic schizophrenic psychoses and schizoaffective psychoses, temporary acute psychotic disorders. Moreover, the invention discloses the use of a pyrimidine derivative known as a COX-2 inhibitor in combination with a neuroleptic drug for the treatment of schizophrenic disorders. Compound preparation is described.

IT 132539-06-1, Olanzapine

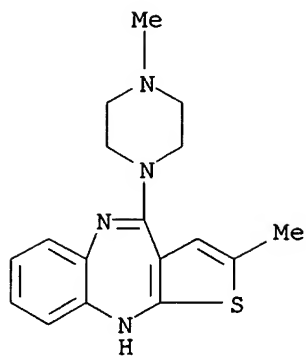
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(cyclooxygenase-2 inhibitors and combinations with neuroleptics for treatment of schizophrenic disorders)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



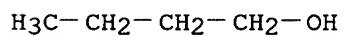
IT **71-36-3**, n-Butanol, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(cyclooxygenase-2 inhibitors and combinations with neuroleptics for treatment of schizophrenic disorders)

RN 71-36-3 CAPLUS

CN 1-Butanol (9CI) (CA INDEX NAME)



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107 ANSWER 4 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:239707 CAPLUS

DOCUMENT NUMBER: 142:254463

TITLE: Dopamine supersensitivity correlates with D2High states, implying many paths to psychosis

AUTHOR(S): Seeman, Philip; Weinshenker, David; Quirion, Remi; Srivastava, Lalit K.; Bhardwaj, Sanjeev K.; Grandy, David K.; Premont, Richard T.; Sotnikova, Tatyana D.; Boksa, Patricia; El-Ghundi, Mufida; O'Dowd, Brian F.; George, Susan R.; Perreault, Melissa L.; Maennistoe, Pekka T.; Robinson, Siobhan; Palmiter, Richard D.; Tallerico, Teresa

CORPORATE SOURCE: Pharmacology Department, University of Toronto, Toronto, ON, M5S 1A8, Can.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2005), 102(9), 3513-3518  
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Dopamine supersensitivity occurs in schizophrenia and other psychoses, and after hippocampal lesions, antipsychotics, ethanol, amphetamine, phencyclidine, gene knockouts of Dbh (dopamine  $\beta$ -hydroxylase), Drd4 receptors, Gprk6 (G protein-coupled receptor kinase 6), Comt (catechol-O-methyltransferase), or Th-/-, DbhTh/+ (tyrosine hydroxylase), and in rats born by Cesarean-section. The functional state of D2, or the high-affinity state for dopamine (D2High), was measured in these supersensitive animal brain striata. Increased levels and higher proportions (40-900%) for D2High were found in all these tissues. If many types of brain impairment cause dopamine behavioral supersensitivity and a common increase in D2High states, it suggests that there are many pathways to psychosis, any one of which can be disrupted.

IT 64-17-5, Ethanol, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (dopamine supersensitivity, D2 states, antipsychotics, and psychosis)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

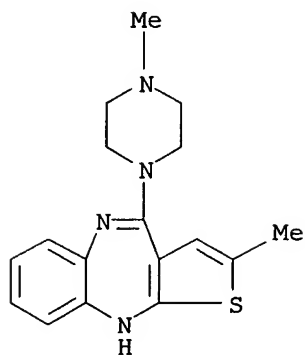
IT 132539-06-1, Olanzapine

RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (dopamine supersensitivity, D2 states, antipsychotics, and psychosis)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)





REFERENCE COUNT:

29

THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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107 ANSWER 5 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:71078 CAPLUS

DOCUMENT NUMBER: 142:183422

TITLE: Prevention of molecular weight reduction of the polymer, impurity formation and gelling in polymer compositions

INVENTOR(S): Thanoo, B. C.; Murtagh, Jim; Johns, Gonto

PATENT ASSIGNEE(S): Oakwood Laboratories, L.L.C., USA

SOURCE: PCT Int. Appl., 114 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005007122	A2	20050127	WO 2004-US23324	20040719
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005042294	A1	20050224	US 2004-894956	20040719
PRIORITY APPLN. INFO.:			US 2003-488573P	P 20030718

AB Polymer and drug containing compns. and method of preparing such compns. are disclosed. The dispersed phase formulation has a polymer, a pharmaceutically or biol. active agent and a small fraction of low pKa acid additive. Stable, filter sterilizable, non-gelling solns. containing e.g. GnRH analogs at least at levels typically used in sustained release formulations and a method of increasing solubility of a high level of a GnRH analog or a freeze-dried antagonist of GnRH in a polymer containing solution

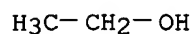
are also disclosed. The amount of the acid additive in the polymer solution is such that it is sufficient to increase the solubility of the high level of the GnRH analog in the polymer solution without affecting the release characteristics of the microspheres prepared therefrom. For example, control of mol. weight (MW) reduction of PLGA in dispersed phase with or without

leuprolide was studied. There was reduction in MW upon incubating the dispersed phase consisting of RG503H, dichloromethane (DCM), and MeOH. The presence of lactic acid, glycolic acid, and oligomer acids reduced the reduction in MW. Under the exptl. conditions, acids with very low pKa, such as lactic (pKa 3.08) and glycolic (pKa 3.83) acids were more effective in preventing MW reduction caused by methanol. Even with a fraction of the acid (less than or equal to 1 mol% to that of the nucleophilic compound, methanol) in the dispersed phase, there was influence on the mol. weight reduction. There was a considerable reduction in the mol. weight of the polymer in

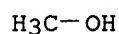
the dispersed phase containing leuprolide. Again, presence of lactic acid, glycolic acid, and oligomer acids reduced the extent of mol. weight reduction, much more efficiently compared to acetic acid.

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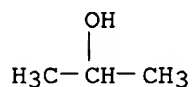
IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses  
67-63-0, Isopropanol, uses 71-23-8, Propanol, uses  
71-36-3, Butanol, uses 75-65-0, tert-Butanol, uses  
RL: NUU (Other use, unclassified); USES (Uses)  
(sustained-release compns. comprising polymer matrix and acid additive  
for preventing polymer mol. weight reduction, impurity formation and gelling  
in presence of nucleophile)  
RN 64-17-5 CAPLUS  
CN Ethanol (9CI) (CA INDEX NAME)



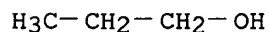
RN 67-56-1 CAPLUS  
CN Methanol (8CI, 9CI) (CA INDEX NAME)



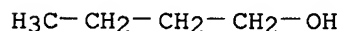
RN 67-63-0 CAPLUS  
CN 2-Propanol (9CI) (CA INDEX NAME)



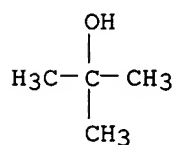
RN 71-23-8 CAPLUS  
CN 1-Propanol (9CI) (CA INDEX NAME)



RN 71-36-3 CAPLUS  
CN 1-Butanol (9CI) (CA INDEX NAME)



RN 75-65-0 CAPLUS  
CN 2-Propanol, 2-methyl- (9CI) (CA INDEX NAME)



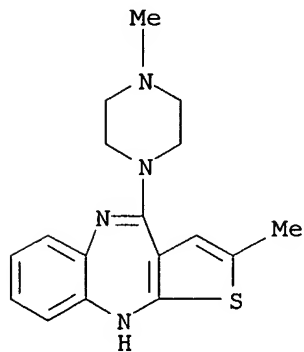
IT 132539-06-1, Olanzapine  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(sustained-release compns. comprising polymer matrix and acid additive

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for preventing polymer mol. weight reduction, impurity formation and gelling  
in presence of nucleophile)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



10/256,198

17 ANSWER 6 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:1122259 CAPLUS

DOCUMENT NUMBER: 142:309676

TITLE: Effects of clozapine, olanzapine and haloperidol on ethanol-induced ascorbic acid release in mouse striatum

AUTHOR(S): Hou, Yue; Yang, Jing Yu; Wu, Chun Fu; Huang, Mei

CORPORATE SOURCE: Department of Pharmacology, Shenyang Pharmaceutical University, Shenyang, 110016, Peop. Rep. China

SOURCE: Progress in Neuro-Psychopharmacology & Biological Psychiatry (2005), 29(1), 83-89

CODEN: PNPPD7; ISSN: 0278-5846

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of clozapine, olanzapine and haloperidol on ethanol-induced striatal ascorbic acid (AA) release in mice were compared by using microdialysis coupled to high performance liquid chromatog. with electrochem. detection. Ethanol (4.0 g/kg i.p.) significantly stimulated striatal AA release by about 200% of baseline in mice. Clozapine and olanzapine, two atypical neuroleptic drugs, at the dose of 1.0 mg/kg s.c., had no effect on basal AA or ethanol-induced AA release. However, both drugs, at the dose of 10 mg/kg s.c., significantly inhibited ethanol-induced AA release. In contrast, haloperidol, a typical neuroleptic drug, at the doses of 0.1-2.0 mg/kg, had no effect on both basal and ethanol-induced AA release. The present study demonstrated that similar actions were exhibited by clozapine and olanzapine, but not by haloperidol, for the regulation of ethanol-induced AA release in the mouse striatum.

IT 64-17-5, Ethanol, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study) (clozapine, olanzapine and 8-hydroxy-2-(di-n-propylamino)tetralin inhibited and haloperidol had no effect on ethanol-induced striatal ascorbic acid release in mouse)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

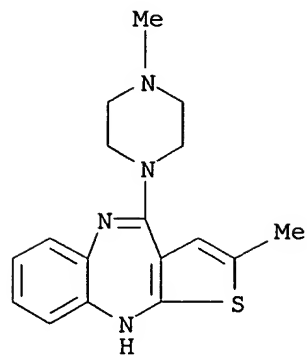
H<sub>3</sub>C-CH<sub>2</sub>-OH

IT 132539-06-1, Olanzapine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (olanzapine at high dose significantly inhibited ethanol-induced striatal ascorbic acid release in mouse)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



REFERENCE COUNT:

49

THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

177 ANSWER 7 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:927215 CAPLUS

DOCUMENT NUMBER: 141:384322

TITLE: Preparation of polymorphic crystalline forms of the antipsychotic agent olanzapine dihydrochloride

INVENTOR(S): Petho, Janos; Barkoczy, Jozsef; Kotay Nagy, Peter; Simig, Gyula; Szent-Kirallyi, Zsuzsa

PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004094433	A1	20041104	WO 2004-HU42	20040422
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: HU 2003-1082 A 20030422

AB Polymorphic crystalline forms of the antipsychotic agent olanzapine dihydrochloride are presented.

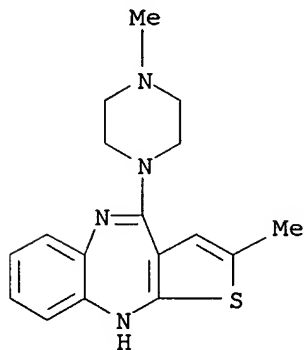
IT 132539-06-1, Olanzapine

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of polymorphic crystalline forms of the antipsychotic agent olanzapine dihydrochloride)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



IT 64-17-5, Ethanol, uses 67-56-1, Methanol, uses 67-63-0, 2-Propanol, uses 71-23-8, 1-Propanol, uses RL: NUU (Other use, unclassified); USES (Uses)

10/256,198

(solvent; in preparation of polymorphic crystalline forms of the antipsychotic

agent olanzapine dihydrochloride)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

$\text{H}_3\text{C}-\text{CH}_2-\text{OH}$

RN 67-56-1 CAPLUS

CN Methanol (8CI, 9CI) (CA INDEX NAME)

$\text{H}_3\text{C}-\text{OH}$

RN 67-63-0 CAPLUS

CN 2-Propanol (9CI) (CA INDEX NAME)

$\begin{array}{c} \text{OH} \\ | \\ \text{H}_3\text{C}-\text{CH}-\text{CH}_3 \end{array}$

RN 71-23-8 CAPLUS

CN 1-Propanol (9CI) (CA INDEX NAME)

$\text{H}_3\text{C}-\text{CH}_2-\text{CH}_2-\text{OH}$

REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/256,198

L2/ ANSWER 8 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:878287 CAPLUS

DOCUMENT NUMBER: 141:360707

TITLE: Treatment of addiction with dopamine receptor antagonists

INVENTOR(S): Horne, Malcolm; Finkelstein, David; Drago, John

PATENT ASSIGNEE(S): Neurosciences Victoria Limited, Australia

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089371	A1	20041021	WO 2004-AU482	20040413
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: AU 2003-901741 A 20030411

AB A method for treating addiction in a mammalian subject comprising administering to the subject an agent capable of inhibiting dopamine receptor activity while maintaining elevated levels of dopamine in the subject.

IT 64-17-5, Alcohol, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (treatment of addiction with dopamine receptor antagonists)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

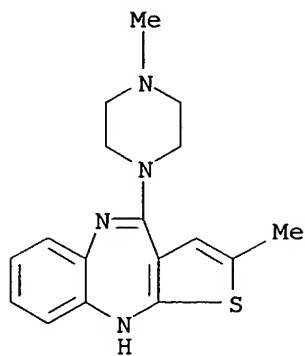
H<sub>3</sub>C-CH<sub>2</sub>-OH

IT 132539-06-1, Olanzapine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (treatment of addiction with dopamine receptor antagonists)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

107 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:872664 CAPLUS

DOCUMENT NUMBER: 141:355325

TITLE: Novel forms of salts, co-crystals, and solvates of olanzapine and uses in treatment of psychosis and functional bowel disorders

INVENTOR(S): Hickey, Magali Bourghol; Remenar, Julius

PATENT ASSIGNEE(S): Transform Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 14

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089313	A2	20041021	WO 2004-US9947	20040331
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
WO 2004078161	A1	20040916	WO 2003-US327772	20030904
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
WO 2004060347	A2	20040722	WO 2003-US341642	20031229
WO 2004060347	A3	20041104		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
WO 2004078163	A2	20040916	WO 2004-US6288	20040226
WO 2004078163	A3	20050120		
W:	AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BY, BY, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,			

IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,  
 LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,  
 MZ, MZ, NA, NI  
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,  
 BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,  
 MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,  
 GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,  
 GQ, GW, ML, MR, NE, SN, TD, TG

## PRIORITY APPLN. INFO.:

US 2003-459501P	P	20030401
US 2003-486713P	P	20030711
US 2003-487064P	P	20030711
WO 2003-US27772	A	20030904
✓US 2003-660202 —	A	20030911
✓US 2003-747742 —	A	20031229
WO 2003-US41642	A	20031229
WO 2004-US6288	A	20040226
US 2004-548343P	P	20040227
✓US 2002-232589 —	A	20020903 6559293
US 2002-437516P	P	20021230
US 2003-441335P	P	20030121
US 2003-451213P	P	20030228
US 2003-378956 —	A	20030303 20030224006
WO 2003-US6662	A	20030303
US 2003-456027P	P	20030318
US 2003-456608P	P	20030321
US 2003-463962P	P	20030418
✓US 2003-449307 —	A	20030530 20046019211
✓US 2003-601092 —	A	20030620 20050025791
WO 2003-US19574	A	20030620
WO 2003-US28982	A	20030916
US 2003-508208P	P	20031002
WO 2003-US41273	A	20031224 20046053853
US 2004-542752P	P	20040206 6699840

AB The invention provides novel soluble forms of olanzapine including novel salts, co-crystals, and solvates of olanzapine. Novel olanzapine forms of the invention are stable, readily formulated, and exhibit improved aqueous solubility when compared to known olanzapine forms. The invention also provides novel pharmaceutical compns. comprising these novel soluble forms and related methods of treatment. Compns. and methods of the invention are useful in the treatment of psychosis and functional bowel disorders, including irritable bowel syndrome.

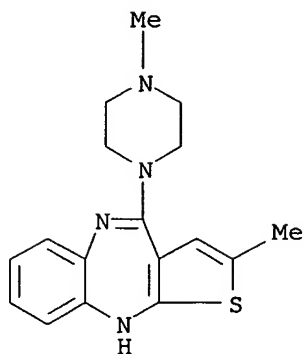
IT 132539-06-1P, Olanzapine

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

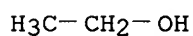
(novel forms of salts, co-crystals, and solvates of olanzapine and uses in treatment of psychosis and functional bowel disorders)

RN 132539-06-1 CAPLUS

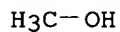
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



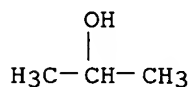
IT 64-17-5, Ethanol, reactions 67-56-1, Methanol, reactions  
 67-63-0, Isopropanol, reactions  
 RL: RGT (Reagent); RACT (Reactant or reagent)  
 (novel forms of salts, co-crystals, and solvates of olanzapine and uses  
 in treatment of psychosis and functional bowel disorders)  
 RN 64-17-5 CAPLUS  
 CN Ethanol (9CI) (CA INDEX NAME)



RN 67-56-1 CAPLUS  
 CN Methanol (8CI, 9CI) (CA INDEX NAME)



RN 67-63-0 CAPLUS  
 CN 2-Propanol (9CI) (CA INDEX NAME)



10/256,198

127 ANSWER 10 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:743280 CAPLUS

DOCUMENT NUMBER: 141:390059

TITLE: Suspected GHB overdoses in the emergency department

AUTHOR(S): Couper, Fiona J.; Thatcher, Jayne E.; Logan, Barry K.

CORPORATE SOURCE: Office of the Chief Medical Examiner, Washington, DC, 20003, USA

SOURCE: Journal of Analytical Toxicology (2004), 28(6), 481-484

CODEN: JATOD3; ISSN: 0146-4760

PUBLISHER: Preston Publications

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Blood specimens from 146 suspected  $\gamma$ -hydroxybutyrate (GHB) overdose cases, presenting to an emergency department in Washington State over a 12-mo period, were analyzed for GHB and other drugs. Of these 146 patients, GHB was confirmed in approx. one-third of the patients (N = 54), sometimes in potentially toxic concns. These patients were aged between 17 and 59 yr (median 28 yr), and 83% were male. Blood GHB concns. ranged from 29 to 490 mg/L (mean 137 mg/L; median 103 mg/L). In 36 (67%) of the 54 patients, other drugs were addnl. detected. Ethanol was measured in 22 (41%) patients, with concns. ranging from 0.01 to 0.26 g/100 mL (median 0.04 g/100 mL). Other commonly co-administered drugs included 3,4-methylenedioxymethamphetamine, marijuana, methamphetamine, cocaine, and citalopram. Frequently observed clin. symptoms on admission for the GHB overdose group included copious vomiting, ataxia, lack of gag reflex, respiratory depression, mild acute respiratory acidosis, unconsciousness, and sudden altered states of consciousness. Many patients required intubation, and several became combative and required restraints. The majority of patients were discharged within 6 h of hospital admission. However, despite presenting with similar clin. symptoms on admission, GHB was not confirmed in 92 of the 146 overdose patients, suggesting that GHB overdose cases may frequently be indistinguishable from other drug overdoses or medical conditions. (c) 2004 Preston Publications.

IT 64-17-5, Ethanol, biological studies 132539-06-1, Olanzapine

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
( $\gamma$ -hydroxybutyrate in blood from suspected overdosed patients in emergency department combined with other drugs and EtOH)

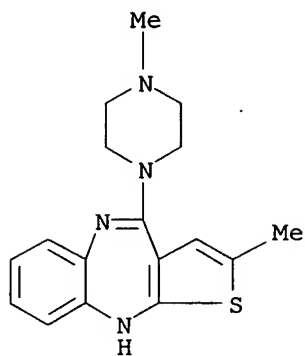
RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



REFERENCE COUNT:

19

THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

127 ANSWER 11 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:566619 CAPLUS

DOCUMENT NUMBER: 141:128822

TITLE: Methods for the preparation of olanzapine hydrate and solvate crystal forms

INVENTOR(S): Dolitzky, Ben Zion; Aronhime, Judith; Diller, Dov

PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.

SOURCE: PCT Int. Appl., 36 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058773	A1	20040715	WO 2003-US41123	20031224
WO 2004058773	C2	20040819		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2004198721	A1	20041007	US 2003-746698	20031224

PRIORITY APPLN. INFO.: US 2002-435913P P 20021224

AB A series of novel crystalline olanzapine forms are prepared and described, in particular hydrated (e.g., olanzapine dihydrate) and solvated crystalline forms of olanzapine (e.g., olanzapine isobutanol solvate).

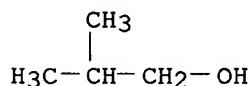
IT 78-83-1, Isobutanol, reactions

RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)

(methods for the preparation of olanzapine hydrate and solvate crystal forms)

RN 78-83-1 CAPLUS

CN 1-Propanol, 2-methyl- (9CI) (CA INDEX NAME)



IT 132539-06-1, Olanzapine

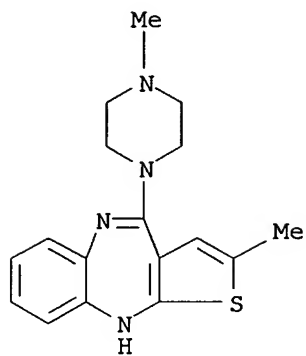
RL: RCT (Reactant); RACT (Reactant or reagent)

(methods for the preparation of olanzapine hydrate and solvate crystal forms)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)





10/256,198

127 ANSWER 12 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:443999 CAPLUS

DOCUMENT NUMBER: 142:192430

TITLE: Fatal blood and tissue concentrations of more than 200 drugs

AUTHOR(S): Musshoff, F.; Padosch, S.; Steinborn, S.; Madea, B.

CORPORATE SOURCE: Institute of Legal Medicine, Rheinische  
Friedrich-Wilhelms-University, Bonn, 53111, Germany

SOURCE: Forensic Science International (2004), 142(2-3),  
161-210

CODEN: FSINDR; ISSN: 0379-0738

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fatal drug concns. in body fluids and tissue samples are presented for more than 200 drugs and chems. of toxicol. interest. Addnl., a reference list is added with more than 600 original papers concerning intoxications with a lethal outcome. The data can be helpful for the interpretation and plausibility control in own cases of intoxication. However, they should be used with caution, because use of drug data without sufficient knowledge about the patient or victim, the circumstances of the case, and about toxicokinetics and toxicodynamics might give a wrong interpretation in a special case.

IT 64-17-5, Ethanol, biological studies 67-56-1, Methanol,  
biological studies 132539-06-1, Olanzapine

RL: ADV (Adverse effect, including toxicity); ANT (Analyte); ANST  
(Analytical study); BIOL (Biological study)

(fatal blood and tissue concns. of more than 200 drugs in humans)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

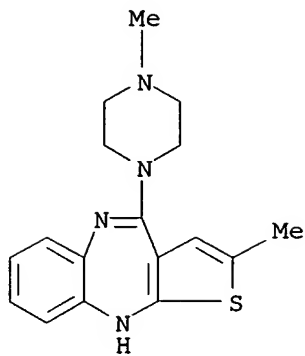
RN 67-56-1 CAPLUS

CN Methanol (8CI, 9CI) (CA INDEX NAME)

H<sub>3</sub>C-OH

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



REFERENCE COUNT:

615 THERE ARE 615 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

10/256,198

107 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:433684 CAPLUS

DOCUMENT NUMBER: 140:429037

TITLE: High viscosity liquid controlled drug delivery system and medical or surgical device

INVENTOR(S): Gibson, John W.; Miller, Stacey S.; Middleton, John C.; Tipton, Arthur J.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 699,002.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004101557	A1	20040527	US 2002-316441	20021210
US 5747058	A	19980505	US 1995-474337	19950607
EP 1525858	A1	20050427	EP 2005-75143	19960607
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6413536	B1	20020702	US 1999-385107	19990827
WO 2004052336	A2	20040624	WO 2003-US39311	20031210
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1995-474337	A2 19950607
			US 1995-478450	B2 19950607
			US 1997-944022	A2 19970915
			US 1999-385107	A3 19990827
			US 2000-699002	A2 20001026
			EP 1996-921521	A3 19960607
			US 2002-316441	A 20021210

AB The present invention relates to novel nonpolymeric compds. and compns. that form liquid, high viscosity materials suitable for the delivery of biol. active substances in a controlled fashion, and for use as medical or surgical devices. The materials can optionally be diluted with a solvent to form a material of lower viscosity, rendering the material easy to administer. This solvent may be water insol. or water soluble, where the water soluble solvent rapidly diffuses or migrates away from the material in vivo, leaving a higher viscosity liquid material. 1,6-Hexanediol lactate  $\epsilon$ -hydroxycaproic acid produced in was dissolved in N-methylpyrrolidone at a weight ratio of 70:30. Bupivacaine base (10%) was then added to this mixture Drops weighing approx. 100 mg were precipitated into 40 mL buffer. At 4 h, around 4.1 weight% of the bupivacaine contained in the precipitated drop had been released. At 24 h, around 8.6 weight% of the bupivacaine had been released.

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IT 64-17-5, Ethanol, biological studies 132539-06-1,  
Olanzapine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(high viscosity liquid controlled drug delivery system and medical or  
surgical device)

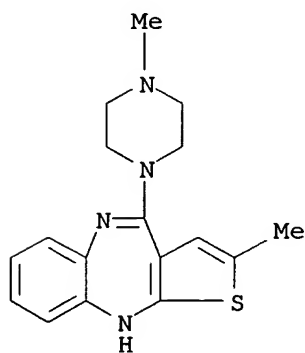
RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

$\text{H}_3\text{C}-\text{CH}_2-\text{OH}$

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



L27 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:354747 CAPLUS

DOCUMENT NUMBER: 140:315112

TITLE: Treating alcohol and/or substance abuse by  
antagonizing  $\alpha$ 2-adrenergic receptors with weak  
dopamine D2 blockadeINVENTOR(S): Green, Alan I.; Keung, Wing Ming; Schidkraut, Joseph;  
Chau, DavidPATENT ASSIGNEE(S): Massachusetts Mental Health Institute, USA; President  
and Fellows of Harvard College

SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004034996	A2	20040429	WO 2003-US32852	20031017
WO 2004034996	A3	20041104		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2502787	AA	20040429	CA 2003-2502787	20031017
PRIORITY APPLN. INFO.:			US 2002-419429P	P 20021018
			WO 2003-US32852	W 20031017

AB Certain atypical antipsychotic medications (particularly clozapine) or combinations of medications are useful to treat alc. or other substance abuse, particularly in the general (non-schizophrenic) population. One aspect of the invention features a method of treating a patient suffering from alc. or other substance abuse by administering to the patient medication effective to rectify an abuse-associated dysfunction in the dopamine-mediated brain reward circuit. A second aspect of the invention features administering medication that strongly antagonizes  $\alpha$ 2-adrenergic receptors and weakly antagonizes dopamine D2 receptors. Preferably, the ratio of  $\alpha$ 2 receptor blockade to D2 receptor blockade is similar to that of clozapine. The medication may be a single compound (e.g. clozapine or risperidone), or it may include two or more compds. which together achieve the specified function. For example, the medication may include a first component which weakly blocks the D2 receptor (e.g. clozapine, quetiapine or ziprasidone or a low dose of another anti-psychotic that is a more potent D2 blocker) and a second component (e.g. clozapine, risperidone or idazoxan) which strongly blocks  $\alpha$ 2 receptors, particularly the  $\alpha$ 2C receptor. Cocktails of the two components are also disclosed.

IT 64-17-5, Ethanol, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) ( $\alpha$ 2-adrenergic receptor antagonism with weak dopamine D2 blockade for treatment of alc. and/or substance abuse)

RN 64-17-5 CAPLUS

10/256,198

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

IT **132539-06-1**, Olanzapine

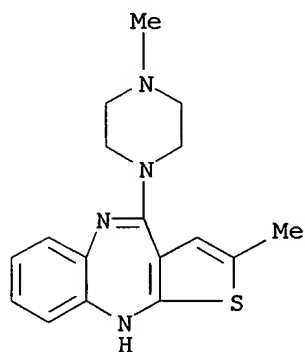
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(α<sub>2</sub>-adrenergic receptor antagonism with weak dopamine D<sub>2</sub> blockade  
for treatment of alc. and/or substance abuse)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



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~~127~~ ANSWER 15 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:203552 CAPLUS

DOCUMENT NUMBER: 140:253583

TITLE: Process of preparation of olanzapine form I

INVENTOR(S): Patel, Hiren V.; Ray, Anup K.; Patel, Pramod B.;  
Patel, Mahendra R.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S.  
Ser. No. 160,958.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004048854	A1	20040311	US 2003-449643	20030530
PRIORITY APPLN. INFO.:			US 2002-160958	A2 20020531

OTHER SOURCE(S): CASREACT 140:253583

AB Disclosed is a process for the preparation of polymorph form I of 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine) by reacting (a) reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and 1-methylpiperazine in an aprotic high boiling solvent or mixts. thereof at a temperature of between about 90 to 130°.; (b) purifying the product of step (a) in an acidic medium; (c) basifying the product of step (b) to a pH of between 7.5-9; and (d) extracting the product of step (c) using a low boiling organic solvent. Olanzapine is known as an antipsychotic agent and polymorph form I is in pharmaceutical formulations.

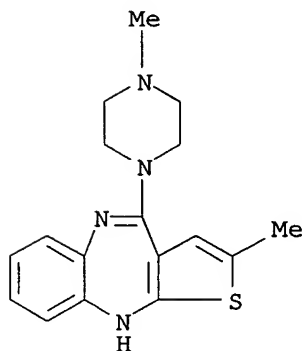
IT **132539-06-1P**, Olanzapine

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(process of preparation of olanzapine polymorph form I by reacting 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and 1-methylpiperazine)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



IT **67-56-1**, Methanol, uses

RL: NUU (Other use, unclassified); USES (Uses)



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(solvent; process of preparation of olanzapine polymorph form I by reacting  
4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine hydrochloride and  
1-methylpiperazine)

RN 67-56-1 CAPLUS

CN Methanol (8CI, 9CI) (CA INDEX NAME)

H<sub>3</sub>C-OH

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L77 ANSWER 16 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60341 CAPLUS

DOCUMENT NUMBER: 140:117406

TITLE: Liquid dosage compositions of stable nanoparticulate drugs

INVENTOR(S): Bosch, William H.; Hilborn, Matthew R.; Hovey, Douglas C.; Kline, Laura J.; Lee, Robert W.; Pruitt, John D.; Ryde, Niels P.; Ryde, Tuula A.; Xu, Shuqian

PATENT ASSIGNEE(S): Elan Pharma International, Ltd, Ire.

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 16

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006959	A1	20040122	WO 2003-US22187	20030716
WO 2004006959	C1	20050331		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2492488	AA	20040122	CA 2003-2492488	20030716
EP 1551457	A1	20050713	EP 2003-764723	20030716
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			US 2002-396530P	P 20020716
			WO 2003-US22187	W 20030716

AB The present invention relates to liquid dosage compns. of stable nanoparticulate drugs. The liquid dosage compns. of the invention include osmotically active crystal growth inhibitors that stabilize the nanoparticulate active agents against crystal and particle size growth of the drug. Thus, an aqueous nanoparticulate colloidal dispersion (NCD) comprising drug 32.5 Copovidone 6.5, and dioctyl sodium sulfosuccinate 0.464% by weight was prepared by milling for 3.8 h under high energy milling conditions. The final mean particle size (by weight) of the drug particles was 161 nm. The concentrated NCD was then diluted with preserved water and glycerol (the osmotically active crystal growth inhibitor) to 0.5-3.0% drug.

IT 64-17-5, Ethanol, biological studies 75-65-0, biological studies 132539-06-1, Olanzapine  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(liquid dosage compns. of stable nanoparticulate drugs)

RN 64-17-5 CAPLUS

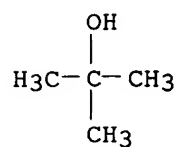
CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

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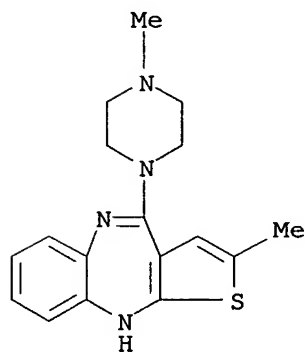
RN 75-65-0 CAPLUS

CN 2-Propanol, 2-methyl- (9CI) (CA INDEX NAME)



RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

L27 ANSWER 17 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:60321 CAPLUS

DOCUMENT NUMBER: 140:117363

TITLE: Preparation of polymorphic forms of olanzapine from its solvates

INVENTOR(S): Kotar, Jordan Berta; Vrecer, Franc; Grcman, Marija

PATENT ASSIGNEE(S): Krka, D.D. Novo Mesto, Slovenia

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

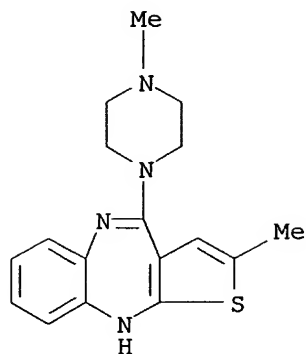
DOCUMENT TYPE: Patent

LANGUAGE: English

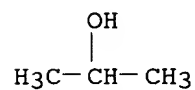
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004006933	A2	20040122	WO 2003-SI24	20030714
WO 2004006933	A3	20040401		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
SI 21270	C	20040229	SI 2002-175	20020715
CA 2493370	AA	20040122	CA 2003-2493370	20030714
EP 1551414	A2	20050713	EP 2003-764287	20030714
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			SI 2002-175	A 20020715
			WO 2003-SI24	W 20030714
AB	The invention relates to a process for the preparation of form I of olanzapine, crystallized from a solvent mixture which comprises 2-propanol, some pseudopolymorphic forms, namely solvates of olanzapine, a new polymorphic form A of olanzapine, and processes for the preparation thereof. For example, form A of olanzapine was prepared by suspending 10.0g olanzapine in 30 mL acetonitrile, adding 35mL methylene chloride in heated suspension, and drying under vacuum at 60OC.			
IT	132539-06-1, Olanzapine RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (polymorphism; preparation of polymorphic forms of olanzapine from its solvates)			
RN	132539-06-1 CAPLUS			
CN	10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)			



IT **67-63-0**, 2-Propanol, processes  
 RL: PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process)  
 (preparation of polymorphic forms of olanzapine from its solvates)  
 RN 67-63-0 CAPLUS  
 CN 2-Propanol (9CI) (CA INDEX NAME)



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107 ANSWER 18 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:2889 CAPLUS

DOCUMENT NUMBER: 140:59669

TITLE: A process for the preparation of olanzapine by direct and reductive methylation of N-demethylolanzapine, and N-demethyl-N-formylolanzapine as an intermediate therefor

INVENTOR(S): Majka, Zbigniew; Stawinski, Tomasz; Rechnio, Justyna; Wieczorek, Maciej

PATENT ASSIGNEE(S): Adamed Sp. Z O.O., Pol.

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

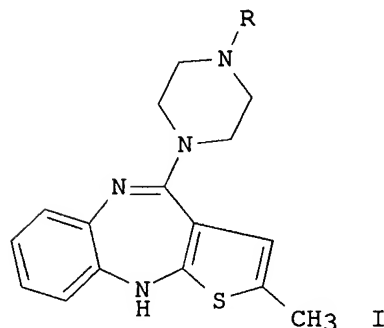
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

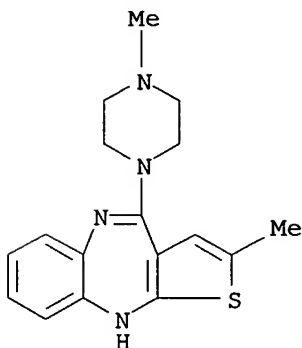
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000847	A1	20031231	WO 2003-IB2181	20030610
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
BR 2003005100	A	20040928	BR 2003-5100	20030610
EP 1513845	A1	20050316	EP 2003-732782	20030610
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
NO 2004000658	A	20040213	NO 2004-658	20040213
PRIORITY APPLN. INFO.:			PL 2002-354642	A 20020620
			WO 2003-IB2181	W 20030610

OTHER SOURCE(S): CASREACT 140:59669

GI



- AB The invention relates to an improved process for the preparation of the CNS drug olanzapine, i.e., I [R = Me] (II). The process consists in N-methylation of N-demethylolanzapine, i.e., I [R = H] (III), which is also named 2-methyl-4-piperazin-1-yl-10H-thieno[2,3-b][1,5]benzodiazepine. The process utilizes several different reactions, including both reductive and direct methylation of III. Advantages of the invention include avoidance of hard-to-remove organic solvents, simpler chemical procedures, high yields, purity as good as the prior art, mild conditions, short reaction times, and low reaction temps. For instance, treatment of III with aqueous formalin in aqueous AcOH containing NaOAc at 0°, followed by treatment with NaBH<sub>4</sub> at 0° under vigorous stirring, gave crude II of 97% purity by HPLC in 97.3% yield. Alternatively, direct methylation of III with MeI and K<sub>2</sub>CO<sub>3</sub> in MeOH at room temperature gave II in 90% purity and 51% yield. The invention also relates to a new intermediate compound, N-demethyl-N-formylolanzapine, i.e., I [R = CHO] (IV), also named 2-methyl-4-(4-formyl-1-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine, and to a process for its preparation. Thus, formylation of III with EtOCHO in refluxing THF gave 72.9% yield of IV, which was reduced with NaBH<sub>4</sub> as above to give II in 88% purity and 86.9% yield. The starting material III was prepared in 85.7% yield by condensation of 4-amino-2-methyl-10H-thieno[2,3-b][1,5]benzodiazepine HCl with piperazine in refluxing PhMe/DMSO mixture
- IT **132539-06-1P**, Olanzapine  
 RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)  
 (improved preparation of olanzapine by methylation or reductive methylation of demethylolanzapine, or via reduction of formyldemethylolanzapine)
- RN 132539-06-1 CAPLUS
- CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



- IT **67-56-1D**, Methanol, arylsulfonate and alkylsulfonate esters  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (methylating agent; improved preparation of olanzapine by methylation or reductive methylation of demethylolanzapine, or via reduction of formyldemethylolanzapine)
- RN 67-56-1 CAPLUS
- CN Methanol (8CI, 9CI) (CA INDEX NAME)

H<sub>3</sub>C—OH

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



10/256,198 ANSWER 19 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:875295 CAPLUS

DOCUMENT NUMBER: 139:354500

TITLE: Novel crystalline polymorph **form VI**  
of olanzapine and a process for its preparation

INVENTOR(S): Reguri, Buchi Reddy; Chakka, Ramesh

PATENT ASSIGNEE(S): Reddy's Laboratories Limited, India; Cord, Janet I.

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

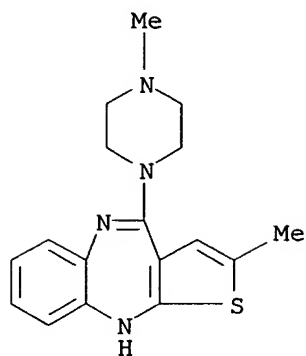
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003091260	A1	20031106	WO 2003-US12414	20030422
WO 2003091260	C2	20040603		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2005153954	A1	20050714	US 2003-509473	20030422
PRIORITY APPLN. INFO.:			IN 2002-MA311	A 20020423
			WO 2003-US12414	W 20030422
AB	A novel crystalline form of 2-methyl-4-(4-methyl-piperazinyl)-10H-thieno[2,3-b][1,5]benzodiazepine (olanzapine), which has a defined X-ray diffraction pattern, is prepared and to its preparation by dissolving olanzapine in a C1-6 alkanol at 0-40° for 30 min to 10 h, isolating the product, and drying it at 40-100°. The olanzapine crystal polymorph is useful for the treatment of CNS disorders (no data).			
IT	132539-06-1, Olanzapine RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (novel crystalline polymorph <b>form VI</b> of olanzapine and a process for its preparation).			
RN	132539-06-1 CAPLUS			
CN	10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)			



REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

197 ANSWER 20 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:796432 CAPLUS

DOCUMENT NUMBER: 139:302061

TITLE: Synergy of dopamine D2 and adenosine A2 receptors  
activates protein kinase A (PKA) signaling via  
 $\beta/\gamma$  dimers, and use in the treatment of  
drug abuse and drug withdrawal

INVENTOR(S): Gordon, Adrienne S.; Diamond, Ivan F.; Yao, Lina

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCT Int. Appl., 152 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082211	A2	20031009	WO 2003-US9629	20030327
WO 2003082211	A3	20041216		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2002-368417P P 20020327

AB The invention pertains to the discovery that a dopamine receptor agonist can activate PKA signaling and/or can act synergistically with an adenosine receptor to activate such signaling. In various embodiments, the invention exploits the synergy between the dopamine receptor pathway and an adenosine receptor pathway to provide methods of mitigating one or more symptoms produced by the chronic consumption of a substance of abuse or to mitigate one or more physiol. and/or behavioral symptoms associated with cessation of chronic consumption of a substance of abuse. In certain embodiments, the methods involve administering to a mammal an effective amount of an adenosine receptor antagonist and an effective amount of a dopamine receptor antagonist, where the effective amount of the adenosine receptor antagonist is lower than the effective amount of an adenosine receptor antagonist administered without the dopamine receptor antagonist.

IT 64-17-5, Ethanol, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(synergy of dopamine D2 and adenosine A2 receptors activates protein  
kinase A signaling via  $\beta/\gamma$  dimers, and use in treatment of  
drug abuse and drug withdrawal)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H3C-CH2-OH

IT 132539-06-1, , Olanzapine

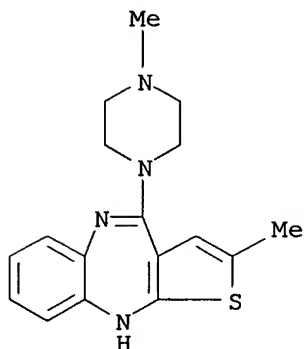
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(synergy of dopamine D2 and adenosine A2 receptors activates protein kinase A signaling via  $\beta/\gamma$  dimers, and use in treatment of drug abuse and drug withdrawal)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



10/256,198

127 ANSWER 21 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:748140 CAPLUS

DOCUMENT NUMBER: 140:264241

TITLE: Olanzapine Reduces Craving for Alcohol: A DRD4 VNTR Polymorphism by Pharmacotherapy Interaction

AUTHOR(S): Hutchison, Kent E.; Wooden, Angela; Swift, Robert M.; Smolen, Andrew; McGeary, John; Adler, Lawrence; Paris, Lyndee

CORPORATE SOURCE: Department of Psychology, University of Colorado at Boulder, Boulder, CO, USA

SOURCE: Neuropsychopharmacology (2003), 28(10), 1882-1888

CODEN: NEROEW; ISSN: 0893-133X

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Sep. investigations have suggested that olanzapine, a D4 antagonist, decreases craving after a priming dose of alc. and that the DRD4 variable number of tandem repeats (VNTR) polymorphism influences the expression of craving after a priming dose of alc. The present study tested the hypothesis that olanzapine may be differentially effective at reducing cue-elicited craving based on individual differences in DRD4 VNTR in a sample of heavy social drinkers. Participants were randomly assigned to receive olanzapine (5 mg) or a control medication (cyproheptadine, 4 mg) prior to consuming three alc. drinks. Participants completed subjective measures of craving and euphoria after each drink. Participants who were homozygous or heterozygous for the 7 (or longer) repeat allele of the DRD4 VNTR were classified as DRD4 L, while the other participants were classified as DRD4 S. The findings indicated that olanzapine reduces craving for alc. at baseline for both DRD4 S and DRD4 L individuals, but only reduces craving after exposure to alc. cues and after a priming dose of alc. for DRD4 L individuals.

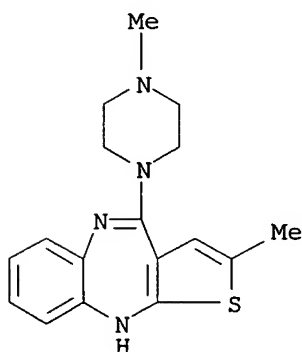
IT 132539-06-1, Olanzapine

RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effect of olanzapine is different at reducing cue-elicited craving based on individual differences in DRD4 VNTR in heavy social drinkers)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



IT 64-17-5, Ethanol, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

10/256,198

(effect of olanzapine is different at reducing cue-elicited craving  
based on individual differences in DRD4 VNTR in heavy social drinkers)  
RN 64-17-5 CAPLUS  
CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 22 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:512084 CAPLUS  
 DOCUMENT NUMBER: 139:74001  
 TITLE: Preparation of crystalline form I of olanzapine  
 INVENTOR(S): Chhabada, Vijay Chhangamal; Rehani, Rajeev Budhdev;  
 Thennati, Rajamamannar  
 PATENT ASSIGNEE(S): Sun Pharmaceutical Industries Limited, India  
 SOURCE: U.S. Pat. Appl. Publ., 6 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003125322	A1	20030703	US 2002-326397	20021223
US 6906062	B2	20050614		
CA 2471341	AA	20030710	CA 2002-2471341	20021223
WO 2003055438	A2	20030710	WO 2002-IN241	20021223
WO 2003055438	A3	20030814		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1470130	A2	20041027	EP 2002-805871	20021223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005513144	T2	20050512	JP 2003-556017	20021223
BE 1015037	A6	20040803	BE 2002-744	20021224
PRIORITY APPLN. INFO.:			IN 2001-MU1211	A 20011224
			WO 2002-IN241	W 20021223

AB Crystalline Form I of olanzapine is characterized by x-ray powder diffraction IR absorbance bands. The compound has a stable color at ambient conditions of storage and its preparation comprises at least 2 repetitive steps of crystallization

from 1 or more organic solvents by dissolving olanzapine in the solvent and allowing crystallization to occur. In at least 1 step the solution is purified by treating with a solid adsorbent material and filtering, and in the last step the cryst.material is subjected to drying. Olanzapine along with 0.75 L of absolute ethanol is stirred at 30°. The contents of the flask are gradually heated to 77-78° to obtain a clear solution and then stirred for 15 mins at 77-78°. Gradually it was allowed to cool to 55-57°. During the process of cooling to 55-57° the solution is seeded with olanzapine Form I at an interval of every 5° until the seed remains undissolved. The contents are further cooled to 30-34° and then to 10°. The solid product is filtered and washed with chilled absolute alc. and sucked dry. The product is dried under vacuum at 47-50° until constant weight to obtain 33 g (yield 66% weight/weight) of Form I.

IT 64-17-5, Ethanol, uses

10/256,198

RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)  
(preparation of crystalline form I of olanzapine)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

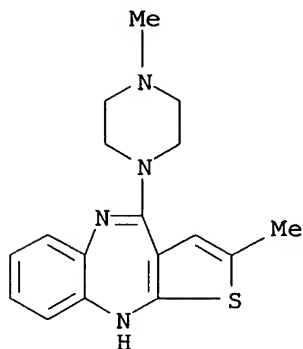
H<sub>3</sub>C-CH<sub>2</sub>-OH

IT **132539-06-1P**, Olanzapine

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PUR (Purification or recovery); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(preparation of crystalline form I of olanzapine)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)





10/256,198

~~L27~~ ANSWER 23 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:319255 CAPLUS

DOCUMENT NUMBER: 138:343854

TITLE: Buccal sprays or capsules containing drugs for treating disorders of the central nervous system

INVENTOR(S): Dugger, Harry A.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. Ser. No. 537,118.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 19

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003077227	A1	20030424	US 2002-230060	20020829
WO 9916417	A1	19990408	WO 1997-US17899	19971001
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
EP 1029536	A1	20000823	EP 2000-109347	19971001
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
EP 1036561	A1	20000920	EP 2000-109357	19971001
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
CA 2497262	AA	20040429	CA 2003-2497262	20030827
WO 2004035021	A2	20040429	WO 2003-US26847	20030827
WO 2004035021	A3	20041111		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
EP 1539106	A2	20050615	EP 2003-796314	20030827
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
US 2004141923	A1	20040722	US 2003-671720	20030929
US 2004265239	A1	20041230	US 2003-671715	20030929
US 2005163719	A1	20050728	US 2003-671709	20030929
US 2004120895	A1	20040624	US 2003-726585	20031204
US 2005002867	A1	20050106	US 2004-834815	20040427
PRIORITY APPLN. INFO.:			WO 1997-US17899	A2 19971001
			US 2000-537118	A2 20000329
			EP 1997-911621	A3 19971001
			US 2002-230060	A 20020829

AB Buccal aerosol sprays or capsules using polar and non-polar solvent have now been developed which provide biol. active compds. for rapid absorption through the oral mucosa, resulting in fast onset of effect. The buccal polar compns. of the invention comprise formulation A: aqueous polar solvent, active compound, and optional flavoring agent; formulation B: aqueous polar solvent, active compound, optionally flavoring agent, and propellant; formulation C: non-polar solvent, active compound, and optional flavoring agent; and formulation D: non-polar solvent, active compound, optional flavoring agent, and propellant. Thus, a lingual spray contained sumatriptan succinate 10-15, EtOH 10-20, propylene glycol 10-15, PEG 35-40, water 10-15, and flavors 2-3%.

IT 64-17-5, Ethanol, biological studies 132539-06-1, Olanzapine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(buccal sprays or capsule containing drugs for treating disorders of central nervous system)

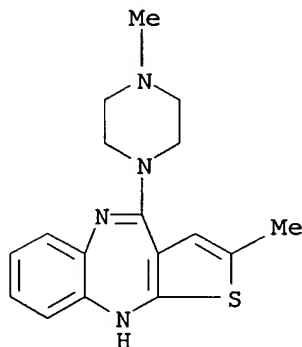
RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



127 ANSWER 24 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:555334 CAPLUS  
 DOCUMENT NUMBER: 137:114525  
 TITLE: Syntactic deformable pharmaceutical foam compositions  
 INVENTOR(S): Odidi, Isa; Odidi, Amina  
 PATENT ASSIGNEE(S): Can.  
 SOURCE: PCT Int. Appl., 47 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002056861	A2	20020725	WO 2002-CA54	20020117
WO 2002056861	A3	20021017		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 6800668	B1	20041005	US 2001-765783	20010119
CA 2435276	AA	20020725	CA 2002-2435276	20020117
CA 2435276	C	20050315		

PRIORITY APPLN. INFO.: US 2001-765783 A 20010119  
 WO 2002-CA54 W 20020117

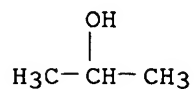
AB The invention relates to methods for preparing a syntactic foam composition suitable for use as a carrier for chems. or other compds., including pharmaceuticals. Carbopol 971P, hydroxyethyl cellulose, cellulose microspheres and silica, was mixed in a high-shear mixer. The resulting admixt. was treated with 2-propanol, while simultaneously subjecting the admixt. to high-shear forces in the high-shear mixer. This mixing created a uniform stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying. Metoprolol succinate was added to the above admixt. and subjected to high-shear agitation for 2 min before treatment with 2-propanol. A stable syntactic deformable and compressible dendritic solid foam which could be shaped before drying was obtained. This was dried at 40°. The dried foam was the disentangled by size reduction to obtain discrete particles. The free flowing particles were reassembled and shaped by compression in a mold. The shaped units, when subjected to an aqueous medium, released metoprolol over a period of ≤3 h.

IT 67-63-0, 2-Propanol, uses  
 RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)  
 (syntactic deformable pharmaceutical foam compns.)

RN 67-63-0 CAPLUS

CN 2-Propanol (9CI) (CA INDEX NAME)

10/256,198



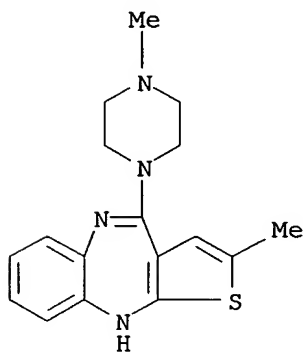
IT 132539-06-1, Olanzapine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(syntactic deformable pharmaceutical foam compns.)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



127 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:539543 CAPLUS

DOCUMENT NUMBER: 137:99017

TITLE: Activated charcoal based composition and method for reducing hangover symptoms associated with the consumption of alcohol containing beverages

INVENTOR(S): Crippen, Raymond L.; Bhargava, Manoj; Morse, Thomas F.

PATENT ASSIGNEE(S): Innovation Ventures, LLC, USA

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002055093	A2	20020718	WO 2002-US625	20020111
WO 2002055093	A3	20030227		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2434388	AA	20020718	CA 2002-2434388	20020111
EP 1349556	A2	20031008	EP 2002-701937	20020111
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004523513	T2	20040805	JP 2002-555827	20020111
PRIORITY APPLN. INFO.:			US 2001-260916P	P 20010112
			WO 2002-US625	W 20020111

AB The invention provides a composition which is effective in the prevention or delay of the onset of side effects associated with alc. consumption or the reduction or alleviation of those effects. The composition of the invention includes activated charcoal and limestone, optionally activated limestone. Optionally, the composition of the invention also includes vitamin B1 and/or other agents such as fatigue relieving agents. Preferably, the composition of the invention is provided in the form of tablets or powder encapsulated in a gelatin capsule. The composition of the invention is provided in pre-dosed quantities varying from between about 100 and 500 mg per dose. The invention also provides a method of reducing or alleviating the deleterious effects associated with alc. consumption. The method includes administration, preferably multiple administration at regularly spaced intervals before, during, and after alc. consumption of a composition containing

activated charcoal and activated limestone.

IT 64-17-5, Ethanol, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (activated charcoals and other actives for reducing hangover symptoms associated with alc. consumption)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

10/256,198

H<sub>3</sub>C-CH<sub>2</sub>-OH

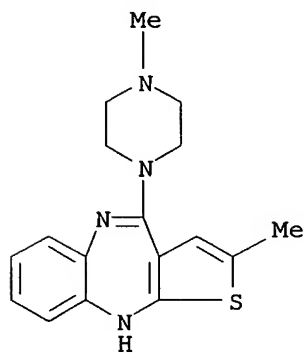
IT 132539-06-1, Olanzapine

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(activated charcoals and other actives for reducing hangover symptoms  
associated with alc. consumption)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



197 ANSWER 26 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:487335 CAPLUS

DOCUMENT NUMBER: 137:68153

TITLE: Novel in-situ forming polymer-based controlled release microcarrier delivery systems

INVENTOR(S): Bhagwatwar, Harshal Prabhakar; Bapat, Varada Ramesh; Paithankar, Mahesh Balkrishna; Yeola, Bhushan Subhash; Gosavi, Arun Shriniwas; Bagool, Manoj Anil; Shetty, Nitin; Shukla, Milind Chintaman; De Souza, Noel John; Khorakiwala, Habil Fakhruddin

PATENT ASSIGNEE(S): India

SOURCE: PCT Int. Appl., 59 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002049573	A2	20020627	WO 2001-IN219	20011214
WO 2002049573	A3	20030130		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2003049320	A1	20030313	US 2001-23427	20011212
CA 2436149	AA	20020627	CA 2001-2436149	20011214
AU 2002022505	A5	20020701	AU 2002-22505	20011214
EP 1363556	A2	20031126	EP 2001-271193	20011214
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			

PRIORITY APPLN. INFO.: US 2000-256319P P 20001218  
WO 2001-IN219 W 20011214

AB A ready-to use, stable, gelled polymer droplet-in-oil dispersion is described which helps in in-situ formation of a multitude of small solid, semisolid, or gelled microcarriers. The dispersion is placed into a body in a semisolid form and cures to form the delivery system in-situ. The process for making such a dispersion comprises the steps of (i) dissolving a polymer in a biocompatible solvent at an elevated temperature to form a polymer solution, (ii) preparing a second oil phase solution of a biocompatible emulsifier at an elevated temperature, (iii) mixing the polymer solution with the oil phase solution at an elevated temperature and subsequently cooling to refrigeration temperature. Placing the gelled dispersion within a body produces the microcarrier delivery system in-situ. The composition of a syringeable, biodegradable dispersion incorporating an effective level of a biol. active agent before injection into a body provides a novel controlled delivery system of drugs for health-care applications. Thus, Poly(DL-lactide-co-glycolide) was dissolved in DMSO to form a polymer solution of a 30% weight/weight concentration. To this solution was added leuprolide acetate to form a 10% weight/weight solution of the drug with respect to the polymer. The

polymer solution was injected by into a continuous oil phase comprising a 20% weight/weight solution of sorbitan monostearate (Arlacel 60) in super refined sesame seed oil maintained at 70-75°, accompanied by high speed homogenization at 13,000 rpm, for 3 min. The resulting polymer droplet-in-oil dispersion was cooled to room temperature with continuous mixing to obtain an opaque mass with a gel-like consistency, which did not flow. The gel was stored under refrigerated conditions until further use. The gel was smooth to the touch with an absence of any gritty particles. Microscopic observation of the gel revealed discrete distorted blue colored droplets of the discontinuous phase dispersed within the continuous oil phase.

IT 64-17-5, Ethanol, uses

RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); PROC (Process); USES (Uses)

(in-situ forming polymer-based controlled release microcarrier delivery systems)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

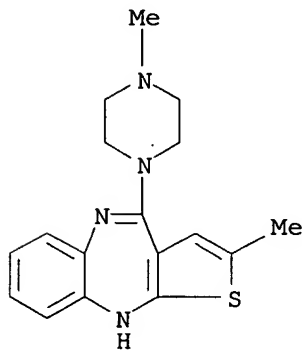
IT 132539-06-1, Olanzapine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in-situ forming polymer-based controlled release microcarrier delivery systems)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)





10/256,198

L27 ANSWER 27 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2002:136045 CAPLUS  
DOCUMENT NUMBER: 136:172816  
TITLE: Polymorphic forms of olanzapine  
INVENTOR(S): Hamied, Yusuf K.; Kankan, Rajendra N.; Rao, Dharmaraj R.  
PATENT ASSIGNEE(S): U & I Pharmaceuticals Ltd., USA  
SOURCE: U.S., 20 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6348458	B1	20020219	US 2000-540749	20000331
IN 187439	A	20020427	IN 1999-BO977	19991228
CA 2395774	AA	20010705	CA 2000-2395774	20001222
WO 2001047933	A1	20010705	WO 2000-GB4982	20001222
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
AU 2001020176	A5	20010709	AU 2001-20176	20001222
AU 779452	B2	20050127		
EP 1246827	A1	20021009	EP 2000-983422	20001222
EP 1246827	B1	20050413		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
DE 20023184	U1	20030508	DE 2000-20023184	20001222
NZ 519926	A	20040227	NZ 2000-519926	20001222
NZ 528520	A	20040827	NZ 2000-528520	20001222
AT 293113	E	20050415	AT 2000-983422	20001222
US 2002165225	A1	20021107	US 2001-26949	20011227
ZA 2002005228	A	20030630	ZA 2002-5228	20020628

PRIORITY APPLN. INFO.:  
IN 1999-BO972 A 19991228  
IN 1999-BO977 A 19991228  
US 2000-540749 A 20000331  
EP 2000-983422 A 20001222  
NZ 2000-519926 A1 20001222  
WO 2000-GB4982 A 20001222

AB The invention provides 3 new polymorphic forms of olanzapine, a process for preparing the new polymorphs and pharmaceutical compns. containing the polymorphs. The new polymorphic forms of olanzapine are useful for the treatment of psychotic conditions, mild anxiety and gastrointestinal conditions. Form I olanzapine (10 g) was dissolved in a mixture of 30 mL HOAc and 30 mL water by stirring. Activated charcoal (0.5 g) was added and the contents filtered over celite. The clear solution was maintained at 20° and 15% aqueous ammonia solution was added over a period of 30 min to adjust the pH to 8. The contents were filtered and dried to obtain Form III olanzapine (9.6 g), which was characterized by IR and XRD.

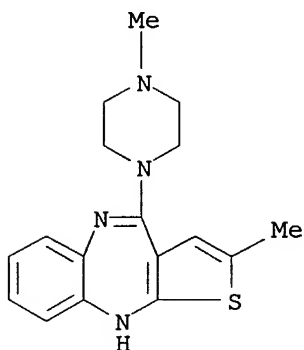
IT 67-56-1, Methanol, uses

10/256,198

RL: NUU (Other use, unclassified); PEP (Physical, engineering or chemical process); PROC (Process); USES (Uses)  
(polymorphic forms of olanzapine)  
RN 67-56-1 CAPLUS  
CN Methanol (8CI, 9CI) (CA INDEX NAME)

H<sub>3</sub>C—OH

IT **132539-06-1**, Olanzapine  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polymorphic forms of olanzapine)  
RN 132539-06-1 CAPLUS  
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

20

THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

127 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:560443 CAPLUS

DOCUMENT NUMBER: 135:338915

TITLE: Optimization of a mathematical topological pattern for the prediction of antihistaminic activity

AUTHOR(S): Duarte, M. J.; Garcia-Domenech, R.; Anton-Fos, G. M.; Galvez, J.

CORPORATE SOURCE: Departamento Ciencias Quimicas, Universidad Cardenal Herrera-CEU, Spain

SOURCE: Journal of Computer-Aided Molecular Design (2001), 15(6), 561-572

CODEN: JCADEQ; ISSN: 0920-654X

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Mol. topol. was used to develop a math. model capable of classifying compds. according to antihistaminic activity. The equations used for this purpose were derived using multi-linear regression and linear discriminant anal. The topol. pattern of activity obtained allows the reliable prediction of antihistaminic activity in drugs frequently used for other therapeutic purposes. Based on the results, the proposed pattern is seemingly only valid for drugs that interact with histamine through competitive inhibition with H1 receptors.

IT 62309-51-7, Propanol 132539-06-1, Olanzapine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(optimization of a math. topol. pattern for the prediction of antihistaminic activity)

RN 62309-51-7 CAPLUS

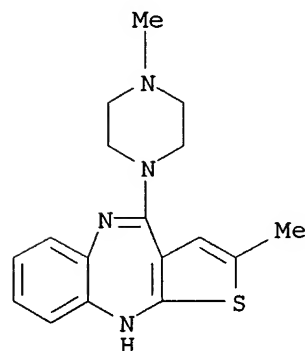
CN Propanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-CH<sub>3</sub>

D1-OH

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



10/256,198

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

L27 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:489405 CAPLUS

DOCUMENT NUMBER: 135:76906

TITLE: Preparation and characterization of new polymorphic crystal forms of olanzapine

INVENTOR(S): Hamied, Yusuf Khwaja; Kankan, Rajendra Narayanrao; Rao, Dharmaraj Ramachandra

PATENT ASSIGNEE(S): Cipla Ltd., India; Wain, Christopher, Paul

SOURCE: PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

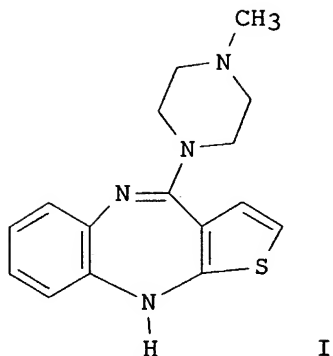
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047933	A1	20010705	WO 2000-GB4982	20001222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 187439	A	20020427	IN 1999-BO977	19991228
US 6348458	B1	20020219	US 2000-540749	20000331
CA 2395774	AA	20010705	CA 2000-2395774	20001222
AU 2001020176	A5	20010709	AU 2001-20176	20001222
AU 779452	B2	20050127		
EP 1246827	A1	20021009	EP 2000-983422	20001222
EP 1246827	B1	20050413		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 519926	A	20040227	NZ 2000-519926	20001222
AT 293113	E	20050415	AT 2000-983422	20001222
ZA 2002005228	A	20030630	ZA 2002-5228	20020628
PRIORITY APPLN. INFO.:			IN 1999-BO977	A 19991228
			US 2000-540749	A 20000331
			IN 1999-BO972	A 19991228
			WO 2000-GB4982	A 20001222

GI



AB Three new polymorphic forms of 2-methyl-4-[4-methyl-1-piperazinyl]-10H-thieno[2,3-b][1,5]benzodiazepine (I; i.e., olanzapine), an antipsychotic (no data) and anxiolytic (no data), are prepared by dissolving the initial I polymorph in aqueous acidic solns. (e.g., AcOH) and precipitating a different I crystal polymorph by neutralization with a base (e.g., aqueous sodium hydroxide). The new polymorphic I forms are characterized via X-ray powder diffraction and FT-IR.

IT **132539-06-1**, Olanzapine

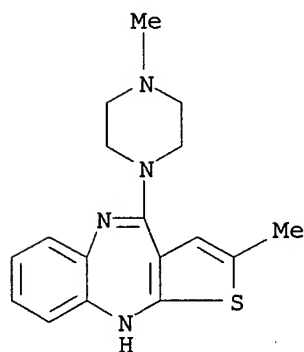
RL: PEP (Physical, engineering or chemical process); PRP (Properties);

PROC (Process)

(preparation and characterization of new polymorphic crystal forms of olanzapine)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



IT **67-56-1**, Methanol, uses

RL: NUU (Other use, unclassified); USES (Uses)

(solvent; preparation and characterization of new polymorphic crystal forms of olanzapine using)

RN 67-56-1 CAPLUS

CN Methanol (8CI, 9CI) (CA INDEX NAME)

H<sub>3</sub>C-OH

10/256,198

REFERENCE COUNT:

5

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

127 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:374858 CAPLUS

DOCUMENT NUMBER: 135:175199

TITLE: Olanzapine reduces urge to drink after drinking cues and a priming dose of alcohol

AUTHOR(S): Hutchison, Kent E.; Swift, Robert; Rohsenow, Damaris J.; Monti, Peter M.; Davidson, Dena; Almeida, Alissa

CORPORATE SOURCE: Department of Psychology, University of Colorado, Boulder, CO, 80309-0345, USA

SOURCE: Psychopharmacology (Berlin, Germany) (2001), 155(1), 27-34

CODEN: PSCHDL; ISSN: 0033-3158

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rationale: Haloperidol, a D2 antagonist, has been shown to moderate the effects of alc. consumption on craving. Objective: The present study was designed to determine whether a single 5-mg dose of olanzapine (a D2/5-HT2 antagonist) would influence responses to alc. cues or an alc. challenge. It was hypothesized that olanzapine would attenuate cue-elicited urge to drink, attenuate the effects of alc. consumption on urge to drink, and reduce the rewarding effects of alc. Methods: To test these hypotheses, 26 heavy social drinkers were randomized to receive either 5 mg olanzapine or placebo approx. 8 h before each of two exptl. sessions. Participants consumed a moderate dose of alc. in one exptl. session and a non-alc. control beverage in another session. Results: Results indicated that mere exposure to alc. cues and consumption of alc. increased urge to drink and that olanzapine attenuated these effects. Results also indicated that alc. increased subjective stimulation and high while olanzapine did not moderate these effects. Conclusions: These results suggest that olanzapine did not influence the rewarding effects of alc. but did attenuate the effects of alc. cues and an alc. challenge on urge to drink.

IT 64-17-5, Ethanol, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(olanzapine reduces urge to drink after drinking cues and priming alc. dose)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

 $\text{H}_3\text{C}-\text{CH}_2-\text{OH}$ 

IT 132539-06-1, Olanzapine

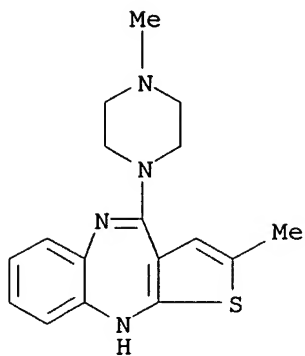
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(olanzapine reduces urge to drink after drinking cues and priming alc. dose)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)





REFERENCE COUNT:

36

THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

107 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:861473 CAPLUS

DOCUMENT NUMBER: 134:32972

TITLE: Porous drug matrixes containing polymers and sugars and methods of their manufacture

INVENTOR(S): Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg

PATENT ASSIGNEE(S): Acusphere, Inc., USA

SOURCE: PCT Int. Appl., 45 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072827	A2	20001207	WO 2000-US14578	20000525
WO 2000072827	A3	20010125		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6395300	B1	20020528	US 1999-433486	19991104
CA 2371836	AA	20001207	CA 2000-2371836	20000525
EP 1180020	A2	20020220	EP 2000-939365	20000525
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
BR 2000010984	A	20020430	BR 2000-10984	20000525
JP 2003500438	T2	20030107	JP 2000-620939	20000525
NZ 516083	A	20030829	NZ 2000-516083	20000525
AU 768022	B2	20031127	AU 2000-54459	20000525
US 2002041896	A1	20020411	US 2001-798824	20010302
US 6610317	B2	20030826		
NO 2001005753	A	20020128	NO 2001-5753	20011126
ZA 2001010347	A	20030730	ZA 2001-10347	20011218
PRIORITY APPLN. INFO.:			US 1999-136323P	P 19990527
			US 1999-158659P	P 19991008
			US 1999-433486	A 19991104
			US 2000-186310P	P 20000302
			WO 2000-US14578	W 20000525

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form,

preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous

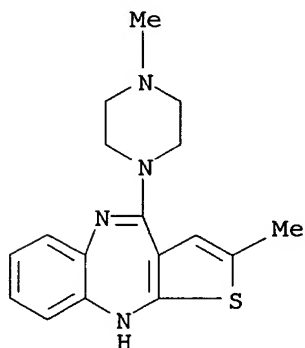
solubility, in

a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably

a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution was prepared by dissolving 3.27 g of  $\text{NH}_4\text{HCO}_3$  and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

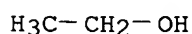
IT **132539-06-1**, Olanzapine  
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

RN 132539-06-1 CAPLUS  
 CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



IT **64-17-5**, Ethanol, biological studies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

RN 64-17-5 CAPLUS  
 CN Ethanol (9CI) (CA INDEX NAME)



10/256,198

127 ANSWER 32 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:725436 CAPLUS

DOCUMENT NUMBER: 133:301171

TITLE: Compositions and methods for improved delivery of ionizable hydrophobic therapeutic agents

INVENTOR(S): Chen, Feng-jing; Patel, Manesh V.

PATENT ASSIGNEE(S): Lipocine, Inc., USA

SOURCE: PCT Int. Appl., 99 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000059475	A1	20001012	WO 2000-US7342	20000316
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 6383471	B1	20020507	US 1999-287043	19990406
CA 2366702	AA	20001012	CA 2000-2366702	20000316
EP 1165048	A1	20020102	EP 2000-916547	20000316
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.:

US 1999-287043

A 19990406

WO 2000-US7342

W 20000316

AB The present invention is directed to a pharmaceutical composition including a hydrophobic therapeutic agent having at least one ionizable functional group, and a carrier. The carrier includes an ionizing agent capable of ionizing the functional group, a surfactant, and optionally solubilizers, triglycerides, and neutralizing agents. The invention further relates to a method of preparing such compns. by providing a composition of an ionizable hydrophobic therapeutic agent, an ionizing agent, and a surfactant, and neutralizing a portion of the ionizing agent with a neutralizing agent. The compns. of the invention are particularly suitable for use in oral dosage forms. A carrier containing concentrated phosphoric acid 0.025,

Tween-20

0.3, Arlacel 186 0.2, sodium taurocholate 0.15, propylene glycol 0.3 g was formulated. Itraconazole was included in the carrier at 30 mg/mL for testing the stability of the itraconazole solution upon dilution in simulated gastric fluid.

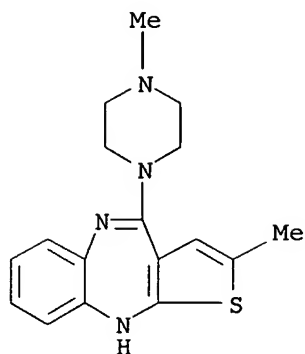
IT 132539-06-1, Olanzapine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

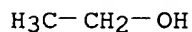
(pharmaceutical compns. containing hydrophobic therapeutic agents and carriers containing ionizing agents and surfactants and triglycerides)

RN 132539-06-1 CAPLUS

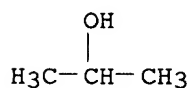
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



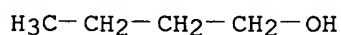
IT 64-17-5, Ethanol, biological studies 67-63-0,  
Isopropanol, biological studies 71-36-3, Butanol, biological  
studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(solubilizer; pharmaceutical compns. containing hydrophobic therapeutic  
agents and carriers containing ionizing agents and surfactants and  
triglycerides)  
RN 64-17-5 CAPLUS  
CN Ethanol (9CI) (CA INDEX NAME)



RN 67-63-0 CAPLUS  
CN 2-Propanol (9CI) (CA INDEX NAME)



RN 71-36-3 CAPLUS  
CN 1-Butanol (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/256,198

~~127~~ ANSWER 33 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:720729 CAPLUS

DOCUMENT NUMBER: 136:256719

TITLE: QSAR model for drug human oral bioavailability.  
[Erratum to document cited in CA133:159633]

AUTHOR(S): Yoshida, Fumitaka; Topliss, John G.

CORPORATE SOURCE: Division of Medicinal Chemistry College of Pharmacy,  
University of Michigan, Ann Arbor, MI, 48109-1065, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(24), 4723  
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB On page 2578, Table 5, the correct footnote e is as follows: "e Weighting is 0.5, where the carbon  $\alpha$  to the carbonyl is tertiary, or the carbonyl is attached to a ring with ortho substituents on each side, or the carbonyl can undergo intramol. hydrogen bonding with a nearby group". On page 2580, in Table 6, under the "structural descriptors" column, the correct data for entries 96 and 133 is 7, 13 for both compds. Under the "drug" column, the correct spelling of the names for entries 83 and 107 are propranolol and chlorthalidone, resp.

IT 64-17-5, Ethanol, biological studies 132539-06-1,  
Olanzapine

RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP  
(Properties); BIOL (Biological study)

(QSAR model for drug human oral bioavailability (Erratum))

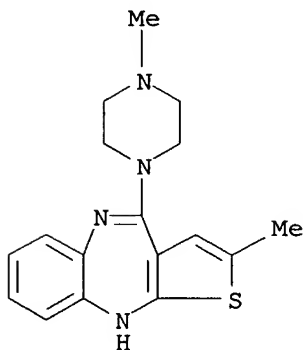
RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



L7 ANSWER 34 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:375684 CAPLUS

DOCUMENT NUMBER: 133:159633

TITLE: QSAR Model for Drug Human Oral Bioavailability

AUTHOR(S): Yoshida, Fumitaka; Topliss, John G.

CORPORATE SOURCE: Division of Medicinal Chemistry College of Pharmacy,  
University of Michigan, Ann Arbor, MI, 48109-1065, USA  
Journal of Medicinal Chemistry (2000), 43(13),  
2575-2585

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The quant. structure-bioavailability relationship of 232 structurally diverse drugs was studied to evaluate the feasibility of constructing a predictive model for the human oral bioavailability of prospective new medicinal agents. The oral bioavailability determined in human adults was assigned one of four ratings and analyzed in relation to physicochem. and structural factors by the ORMUCS (ordered multicategorical classification method using the simplex technique) method. A systematic examination of various physicochem. parameters relating primarily to absorption, and structural elements which could influence metabolism, was carried out to analyze their effects on the bioavailability classification of drugs in the data set. Lipophilicity, expressed as the distribution coefficient at pH 6.5, was found to be a significant factor influencing bioavailability. The observation that acids generally had better bioavailability characteristics than bases, with neutral compds. between, led to the formulation of a new parameter,  $\Delta \log D$  ( $\log D_{6.5} - \log D_{7.4}$ ), which proved to be an important contributor in improving the classification results. The addition of 15 structural descriptors relating primarily to well-known metabolic processes yielded a satisfactory QSAR equation which had a correct classification rate of 71% (97% within one class) and a Spearman rank correlation coefficient ( $R_s$ ) of 0.851, despite the diversity of structure and pharmacol. activity in the compound set. In leave-one-out tests, an average of 67% of drugs were correctly classified (96% within one class) with an  $R_s$  of 0.812. The relationship formulated identified significant factors influencing bioavailability and assigned them quant. values expressing their contribution. The predictive power of the model was evaluated using a sep. test set of 40 compds., of which 60% (95% within one class) were correctly classified. Since the necessary physicochem. parameters can be calculated or estimated and the structural descriptors are obtained from an inspection of the structure, the model enables a rough estimate to be made of the prospective human oral bioavailability of unsynthesized compds. Also, the model has the advantage of transparency in that it indicates which factors may affect bioavailability and the extent of that effect. This could be useful in designing compds. which are more bioavailable. Refinement of the model is possible as more bioavailability data becomes available. Potential uses are in drug design, prioritization of compds. for synthesis, and selection for detailed studies of early compound leads in drug discovery programs.

IT 64-17-5, Ethanol, biological studies 132539-06-1,  
Olanzapine

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(QSAR model for drug human oral bioavailability)

RN 64-17-5 CAPLUS

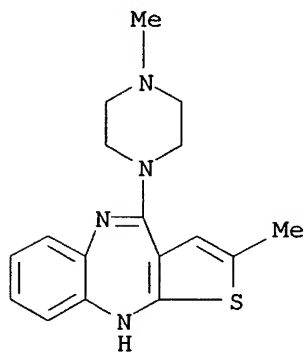
CN Ethanol (9CI) (CA INDEX NAME)

10/256,198

H<sub>3</sub>C-CH<sub>2</sub>-OH

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)



REFERENCE COUNT:

38

THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



L27 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:653544 CAPLUS

DOCUMENT NUMBER: 129:286009

TITLE: 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine for treatment of psychoactive substance disorders

INVENTOR(S): Beasley, Charles M., Jr.; Chakrabarti, Jiban Kumar; Hotten, Terrence Michael; Tupper, David Edward

PATENT ASSIGNEE(S): Eli Lilly and Company, USA; Eli Lilly and Company Limited

SOURCE: U.S., 10 pp., Cont.-in-part of U.S. 5,605,897.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5817657	A	19981006	US 1996-748294	19961113
US 5229382	A	19930720	US 1992-890348	19920522
US 5605897	A	19970225	US 1995-387498	19950213

PRIORITY APPLN. INFO.:

US 1991-690143	A1	19910423
US 1992-890348	A2	19920522
US 1993-44844	B2	19930408
US 1995-387498	A2	19950213
GB 1990-9229	A	19900425

AB 2-Methyl-4-(4-methyl-1-piperazinyl)-10H-thieno-[2,3-b][1,5]benzodiazepine (preparation described), or an acid salt thereof, has pharmaceutical properties, and is of particular use in the treatment of disorders relating to the use of psychoactive substances.

IT 64-17-5, Ethanol, biological studies

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (alc. withdrawal delirium and hallucinosis and dementia;

methyl(methylpiperazinyl)thienobenzodiazepine, preparation, pharmaceutical formulations, and treatment of psychoactive substance disorders)

RN 64-17-5 CAPLUS

CN Ethanol (9CI) (CA INDEX NAME)

H<sub>3</sub>C-CH<sub>2</sub>-OH

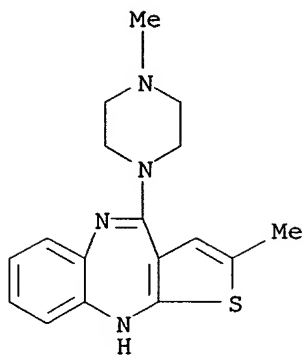
IT 132539-06-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(methyl(methylpiperazinyl)thienobenzodiazepine, preparation, pharmaceutical formulations, and treatment of psychoactive substance disorders)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-(9CI) (CA INDEX NAME)



REFERENCE COUNT:

14

THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:623041 CAPLUS  
 DOCUMENT NUMBER: 127:244231  
 TITLE: Method for treating substance abuse  
 INVENTOR(S): Beasley, Charles M., Jr.; Rasmussen, Kurt; Tollefson, Gary D.  
 PATENT ASSIGNEE(S): Eli Lilly and Company, USA  
 SOURCE: PCT Int. Appl., 31 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733586	A1	19970918	WO 1997-US3404	19970310
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2248738	AA	19970918	CA 1997-2248738	19970310
AU 9720672	A1	19971001	AU 1997-20672	19970310
AU 725940	B2	20001026		
CN 1213308	A	19990407	CN 1997-193069	19970310
BR 9708037	A	19990727	BR 1997-8037	19970310
EP 1007050	A1	20000614	EP 1997-908871	19970310
EP 1007050	B1	20050518		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
NZ 331845	A	20000929	NZ 1997-331845	19970310
JP 2000517287	T2	20001226	JP 1997-522340	19970310
AT 295731	E	20050615	AT 1997-908871	19970310
US 6159963	A	20001212	US 1997-952845	19971125
NO 9804196	A	19981103	NO 1998-4196	19980911
PRIORITY APPLN. INFO.:			US 1996-13160P	P 19960311
			US 1996-13161P	P 19960311
			GB 1996-6615	A 19960329
			GB 1996-6617	A 19960329
			WO 1997-US3404	W 19970310
AB	The invention provides a method for treating substance abuse comprising administering an effective amount of olanzapine or pharmaceutically acceptable salt thereof to a patient in need thereof.			
IT	64-17-5, Ethanol, biological studies			
	RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (dependence; olanzapine for treating substance abuse)			
RN	64-17-5 CAPLUS			
CN	Ethanol (9CI) (CA INDEX NAME)			

H<sub>3</sub>C-CH<sub>2</sub>-OH

IT 132539-06-1, Olanzapine

10/256,198

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(olanzapine for treating substance abuse)

RN 132539-06-1 CAPLUS

CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-  
(9CI) (CA INDEX NAME)

